IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Galla Chandra Rao et al.

Serial No. 10/706,108

Filed: 11/12/2003

For: Labeled Cell Sets for Use as Functional Controls in Rare Cell Detection Assays.

Examiner: Karen A. Canella

Group Art Unit: 1643

Response to 09/25/2006 Office Action

Our File No.: IMMC 234.1

RESPONSE

Claim Rejection under 35 USC § 112

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph as not reasonably providing enablement for an improvement which is using two or more populations of control cells having different fluorescent markers at the same intensity to spike a patient sample at the same concentration.

#1 Response:

The sets are defined as separate populations based upon the cell number (page 18; lines 6-9). Example 10 describes internal controls at different cell concentrations (page 41; line 11 to page 44; line 2). Applicant has amended independent claim 1 and claim 15 to sets of control cells at different concentrations as further supported in the specifications (page 12; line 26-27).

A) Addition of two fluorescently distinct control cell populations in an external control. Claims 5 and 17 specify that the cell populations are external control cells.

The specification provides no teachings as to how the presence of two fluorescently distinct control cell populations would constitute an improvement over the prior art when used as an external control.

#2 Response:

External control cells are not useful in assessing random errors, but would be appropriate in determining systemic errors (page 17, lines 17-22). Yet unlike manual assay methods, external control cells in automated instruments would be useful in assessing systemic errors in an automated system (page 21, lines 22-24). Accordingly, there is a need in automated systems, designed for rare cell analysis as described in US 6,365,362 (page 19, line 26-28), to provide an external control. Two separate populations of control cells within the same sample are used to eliminate any potential differences in the density of target cells that may be outside an expected predetermined antigen density of a single population of control cells (page 23, lines 22-27). In cancer cells and as shown in Figure 3, the antigen densities of several cancer cell lines vary and reflect the antigen density of the tumor cells actually found in breast cancer patients (page 23, line 7-10). Because of this, the proportion of a single control cell recovered may not reflect the proportion of cancer cells present in a sample. This is especially true when dealing with rare events. Consequently, the recovery of two cell lines compensates for differences in antigen density (page 23, line 12-14) and provides confidence in the assessment of target cells.

Applicant submits that the simultaneous use of two fluorescently distinct control cell populations as external controls provides improvement upon the prior art by ensuring that any differences in an automated process for the recovery of tumor cells having varying densities are considered within a range which provides confidence in rare cell quantitation. This is especially true when not using the controlled aggregation technique, described in US 6,623,982 (page 23, line 16-20). Accordingly, applicant has amended independent claims 5 and 17 to limit the external control cells to automated detection and enrichment processes.

B) <u>Addition of two fluorescently distinct control cell populations in an internal control.</u>

The specification does not teach any improvement associated with the inclusion of control cell populations with the same fluorescent intensity, or the inclusion of distinct control cells at the same concentration in the patient sample.

#3 Response:

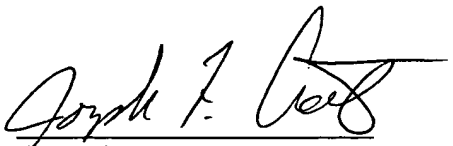
Applicant has limited the scope of enablement in the claims to better reflect the scope set forth in the specifications by limiting the claims 1 and 15 to distinct sets with different intensities at different concentrations.

Nonstatutory double patenting of co-pending application 09/801,471.

Applicant has submitted a terminal disclaimer in compliance with 37CFR 1.321(c) or 1.321(d). The terminal disclaimer fee as determined under 37 CFR 1.20(d) is included.

By the attached amendments, applicants have amended the claims to define the invention more particularly and distinctly so as to overcome the rejections and to patentably define the invention over the prior art. In view of these amendments and related discussions and arguments, it is respectfully urged that the rejections set forth in the 09/25/2006 Office Action should be withdrawn and that this application be passed to issue. In the event the examiner has any comments or questions, the examiner is invited to telephone or e-mail applicants' undersigned representative at the number below.

Yours Respectfully,



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